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10/594,453	09/26/2006	Michael Kretschmar	LNK-019	1342

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EXAMINER	
TSAY, MARSHA M	

ART UNIT	PAPER NUMBER
1656	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/594,453	KRETSCHMAR ET AL.	
	Examiner	Art Unit	
	Marsha M. Tsay	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 January 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

This Office action is in response to Applicants' remarks received January 12, 2009.

Applicants' arguments have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous Office actions are hereby withdrawn.

Claims 1-24 are currently under examination.

Priority: The request for priority to GERMANY 102004044429.3, filed September 14, 2004, is acknowledged.

Objections and Rejections

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3-5, 10-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zykova et al. (1983 Voprosy Meditsinskoi Khimii 25(5): 114-117 abstract; IDS, previously cited). Zykova et al. disclose a method for the precipitation of fibronectin from a plasma fraction using 0.8 to 2.0 M (800 to 2000 mM) at a pH 5.0 (abstract). The fibronectin precipitate of Zykova et al. contained at least 80% fibronectin (since Zykova et al. disclose fibronectin loss was about 20%).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to separate fibronectin by the method of Zykova et al. such that the fibronectin precipitate contains at least 80% fibronectin (claims 1, 3-5, 10-11). Regarding the ionic strength (the instant ionic strength is below 500 mM), it should be noted that generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be *prima facie* obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); see also *Peterson*, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."); *In re Hoeschele*, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969). For more recent cases applying this principle, see *Merck & Co. Inc. v. Biocraft Laboratories Inc.*, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), *cert. denied*, 493 U.S. 975 (1989); *In re Kulling*, 897 F.2d 1147, 14 USPQ2d 1056 (Fed. Cir. 1990); and *In re Geisler,* 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997).

In their remarks, Applicants assert that Zykova discloses the preparation of fibronectin from bovine blood serum, obtained by means of affinity chromatography on collagen separation, through "differential salting out", using high concentrations of ammonium sulfate ranging from 0.8 to 2.0 M (800 to 2"00 mM) at a pH 5.0. In contrast, the pending claims require low salt concentrations, using a plasma fraction that is "characterized by an ionic strength below 500 mM." Applicant's arguments have been fully considered but they are not persuasive.

Firstly, the Zykova et al. reference has been withdrawn as a 35 U.S.C. 102(b) reference and is now applied as a 103(a) reference.

Secondly, the use of open claim language "comprising" allows for anticipation of additional steps and/or elements. Regardless of the additional steps and/or elements disclosed by Zykova et al., Zykova et al. still disclose claim 1(i) wherein a fibronectin precipitate is formed and then separated from a coagulation factor.

Regarding, Applicants' introduction of the limitation (i.e. an ionic strength below 500 mM), it should be noted that generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." See also the 103(a) rejection of Zykova et al.

At least for these reasons, the Zykova et al. reference is still believed to be relevant art under 103(a).

Claims 1-5, 6, 8-13, 14, 16, 18-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wallace et al. (US 4341764; previously cited). Wallace et al. disclose a method for preparing fibronectin and antihemophilic factor from blood plasma comprising the steps of: forming a solution of blood plasma fraction in an aqueous medium, acidifying the solution to a pH sufficient to form an acid precipitate, separating the acid-precipitate from the solution, isolating fibronectin from the precipitate, and isolating antihemophilic factor from the solution at a temperature of 2°-20° C (col. 9-10 lines 1-21; claims 1-5, 10-11, 16, 18-24). Wallace et al. further disclose that the solution can be acidified at a pH of about 5.0 to form the acid precipitate (col. 9 line 13; claims 1-5, 10-11). Wallace et al. also disclose the plasma fraction is dissolved cryoprecipitate (col. 9 line 9, col. 5 line 28; claim 14). In Example 1, Wallace et al. disclose the acid precipitate contains 260 g protein (col. 5 line 34; claim 8). After precipitation, the precipitate suspension was stirred for 3 hours (col. 5 lines 50-53; claim 6). In col. 4, lines 40-42, Wallace et al. disclose that the precipitate contains a major proportion of the fibronectin (i.e. greater than 50%, preferably greater than 60%).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to separate fibronectin and/or a coagulation factor from a plasma fraction by the method of Wallace et al. as noted above and such that the major proportion of the fibronectin precipitate is composed of fibronectin, (i.e. greater than 60%, 70%, etc.) (claims 1-5, 6, 8, 10-11, 14, 16, 18-24). Since Wallace et al. disclose that the percentage of fibronectin in said precipitate is preferably greater than 60%, it would be reasonable for one of ordinary skill to accept that said fibronectin precipitate of Wallace et al. can contain up to 70%, 80%, and even 90% of fibronectin since the range of greater than 60% is disclosed. Further, one of ordinary skill would

recognize that plasma naturally contains the components of natural salts, i.e. NaCl or KCl, and amino acids, i.e. glycine (claims 9, 12-13).

In the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a *prima facie* case of obviousness exists. *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976); *In re Woodruff*, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990) (The prior art taught carbon monoxide concentrations of "about 1-5%" while the claim was limited to "more than 5%." The court held that "about 1-5%" allowed for concentrations slightly above 5% thus the ranges overlapped.)". Similarly, a *prima facie* case of obviousness exists where the claimed ranges and prior art ranges do not overlap but are close enough that one skilled in the art would have expected them to have the same properties. *Titanium Metals Corp. of America v. Banner*, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985).

In their remarks, Applicants assert that (1) in order for a reference to anticipate, it must disclose each and every element of the pending claims. Wallace discloses a complex, multi-step process for the preparation of fibronectin and fibronectin substitutes from an acid-chill precipitate. Thus, the Wallace process involves the use of several distinct steps, including multiple centrifugation steps, to obtain a purified fibronectin substitute precipitate. (2) Wallace requires further cooling steps to precipitate the remaining fibronectin and even then only permits the capture of greater than 50%, possibly greater than 60% of the fibronectin present in the original plasma fraction. In contrast to Wallace, the invention of the pending claims relates to a simple, one-step titration process that results in the direct quantitative separation of fibronectin from a plasma solution to yield a purified coagulation factor, (i.e. vWF), a process that results in

the high yield recovery of 70% to 90%, more preferably at least 90% of the fibronectin present in the plasma fraction. Applicant's arguments have been fully considered but they are not persuasive.

Firstly, it should be noted that the Wallace et al. reference has been withdrawn as a 35 U.S.C. 102(b) reference and is now applied as a 103(a) reference.

(1a) Applicants are reminded the use of open claim language "comprising" allows for anticipation of additional steps and/or elements. Regardless of the additional steps disclosed by Wallace et al., Wallace et al. still discloses step (i) as recited in claims 1 and 2 wherein a fibronectin precipitate is formed and then separated from a coagulation factor.

(2a) Wallace et al. disclose the fibronectin precipitate contains a major proportion of fibronectin, i.e. greater than 50%, preferably greater than 60% (col. 4 lines 40-42). As noted in the 103(a) rejection above, it would be reasonable for one of ordinary skill to expect that a fibronection precipitate having greater than 50% or 60% fibronectin would encompass the values of up to 70%, 80%, 90% fibronectin.

For at least these reasons, the Wallace et al. reference is still believed to be relevant art under 103(a).

Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Wallace et al. (US 4341764). The teachings of Wallace et al. are outlined above. Wallace discloses the acid-precipitate was separated by centrifugation. Wallace et al. do not teach separation by means of an agitator blade of a stirrer.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to recognize that the separation of the acid-precipitate from the plasma fraction can be done by any acceptable means known in the art, i.e. the blade of a stirrer, since techniques for separating a precipitate from a solution are routine in the art (claim 7).

Applicants remarks regarding the Wallace et al. has been considered but are not found to be persuasive.

The reasons for maintaining the Wallace et al. reference is the same as noted above.

Claims 15, 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wallace et al. (US 4341764; previously cited) in view of Burnouf-Radosevich et al. (US 5408039; previously cited). The teachings of Wallace et al. are outlined above. Wallace et al. do not teach purification steps of the cryoprecipitated plasma fraction or vWF.

Burnouf-Radosevich et al. disclose a process for purifying human von Willebrand factor (vWF) from a cryoprecipitated plasma fraction, which comprises a series of purification steps (col. 5-7). Burnouf-Radosevich et al. disclose aluminum hydroxide treatment to remove fibronectin (col. 5 lines 43-49), a solvent-detergent treatment to destroy lipid enveloped viruses (col. 5 lines 57-60), and an anion exchange chromatographic step (col. 6). After the anion exchange chromatographic step, Burnouf-Radosevich et al. disclose that the vWF eluate reveals a slight contamination by fibronectin (col. 6 lines 66-68).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the teachings of Wallace et al. by substituting the purification steps of

Burnouf-Radosevich et al. to a plasma fraction for the separation of fibronectin and a coagulation factor (vWF) (claims 15, 17). The motivation to do so is given by Burnouf-Radosevich et al., which discloses further purification steps of plasma fraction in the separation of fibronectin and a different coagulation factor than that of Wallace et al. (i.e. vWF). It would be reasonable for one of ordinary skill to recognize that additional purification steps of Burnouf-Radosevich et al. would yield a purer protein product and that since Wallace et al. already disclose the separation of a coagulation factor; a specific factor (i.e. vWF) can therefore be separated.

Applicant's arguments, respect to claims 9, 12-13, 15-17 as being unpatentable over Burnouf-Radosevich et al. (US 5408039) in view of Winkelman (US 4789733) have been fully considered and are persuasive. The rejection of claims 9, 12-13, 15-17 as being unpatentable over Burnouf-Radosevich et al. (US 5408039) in view of Winkelman (US 4789733) has been withdrawn.

However, claims 15, 17 remain rejected in the newly cited 103(a) rejection as being unpatentable over Wallace et al. in view of the Burnouf-Radosevich et al. The reasons for maintaining the Wallace et al. reference is the same as noted above.

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marsha M. Tsay whose telephone number is (571)272-2938. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would

like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Maryam Monshipouri/

Primary Examiner, Art Unit 1656

January 23, 2009